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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/523,784

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EXAMINER

LUM, LEON YUN BON

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1641

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/523,784	Applicant(s) METHFESSEL ET AL.	
	Examiner Leon Y. Lum	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 April 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-20 is/are pending in the application.
- 4a) Of the above claim(s) 14 and 18-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-13 and 15-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/2/09, 4/1/09</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicants' election with traverse of Group I, claims 11-17 and the species connexin and supported bilayer in the reply filed on June 30, 2008 is acknowledged. Applicants traversed by setting for a series of arguments. See pages 3-4.

Applicants first argue that the elements in List II should not have been restricted, citing MPEP § 1850(II). See page 3. This section of the MPEP, however, is directed to a restriction based on a lack of unity, not a species election, which is the subject of List II. As stated in the Office Action, the appropriate authority is PCT Rule 13.1 and 13.2, which state that a species election is appropriate if the species lack the same or corresponding special technical features. Here, because the three listed species, i.e., supported bilayer, membrane covers end of a capillary, and living cell, lack the same special technical features, a requirement to elect one of them is proper. The species election requirement is therefore maintained and made FINAL.

Applicants then argue that, with respect to List I, connexins and innexins are functionally similar alternatives and should be examined together. See page 3. With respect to List I, Applicants' arguments are convincing and the species are REJOINED.

Information Disclosure Statement

The Examiner appreciates Applicants submitting the missing references mentioned in the previous Office Action and for disclosing that the "AD" reference may

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not exist. If the reference does not exist, then mention of it should be removed from the specification. Because it isn't clear that the alternative citations (2 and 3 on the IDS filed February 2, 2009) are the originally intended document, they are not considered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

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not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-12 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mazet *et al.* (Eur. J. Biochem., 210, 249-256 (1992)) ("Mazet") in view of Barbier *et al.* (US 2004/0126817) ("Barbier").

i. Independent claim 11 is obvious

Mazet teaches a planar lipid-bilayer membrane stretched across a hole in a partition separating two chambers. See page 251, left column, last paragraph. The membrane comprises connexin-32, which is incorporated therein by contacting the membrane with a proteoliposome preparation comprising the protein. See page 252, left column, first full paragraph. Mazet, therefore, teaches "a membrane," as claimed. Mazet also teaches that channel activity attributed to connexin-32 can be detected by measuring current in response to voltage input. *Id.* at second full paragraph. Mazet, therefore, teaches "an electrical measuring instrument" and "electrodes" (claim 11) and the "providing" and "measuring" steps (claims 15 and 17), as claimed.

Mazet, however, does not teach a membrane body comprising at least one connexin or innexin.

Barbier teaches an assay to investigate gap junction intercellular communication, which includes contacting two embodiments comprising connexins. See page 2, paragraph 0010. In particular, Barbier discloses that the embodiments are cells. *Id.*

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to modify Mazet's arrangement by including a cell comprising connexins. The modification would produce contact between Mazet's lipid bilayer comprising connexin-32 and Barbier's cell comprising connexins. The skilled artisan would have made the modification because both Mazet and Barbier are directed to intercellular gap junctions comprising connexins, and substituting a cell for a membrane is not inventive since the same type of gap junction is maintained. For this reason, the skilled artisan would have had a reasonable expectation of success in combining the references. If evidence can be provided to the contrary, then the rejection may be withdrawn.

ii. Dependent claims 12 and 15-17 are obvious

Regarding claims 2 and 15, these limitations are described above. *See supra* rejection of claim 11.

Regarding claim 16, Mazet teaches the step of measuring current. *See page 252, left column, second full paragraph.*

Regarding claim 17, Barbier teaches the step of providing a test compound, in order to determine its affect on altering properties of the gap junction. *See page 2, paragraph 0018-0019.*

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mazet in view of Barbier, both cited above, as applied to claim 11 above, and further in view of Xu *et al.* (US 5,874,668) ("Xu").

The teachings of Mazet and Barbier are disclosed above. These references do not, however, teach a membrane that covers an end of a capillary as claimed.

Xu describes a reconstituted membrane placed the end of a patch clamp electrode. See column 9, lines 35-39 and 54-65; and Figure 4D. This configuration allows one to understand adhesion forces between two surfaces and enables one to simultaneously image receptor structure and record single and multiple channel conductances. *Id.*

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to place Mazet and Barbier's connexin-32 incorporated membrane at the end of a patch clamp electrode. As evidenced by Xu, the skilled artisan would have been motivated to perform this modification since such an arrangement would allow one to understand adhesion forces between the bilayer membrane and cell, and also allow simultaneous measurements of single and multiple channel conductances. Moreover, since the patch clamp arrangement would allow the same type of conductance measurements taught by Mazet, the skilled artisan would have had a reasonable expectation of success in combining the teachings of Mazet and Barbier with the teachings of Xu.

Response to Arguments

Applicants traverse the rejection of claims 11-13 and 15-17 in the Response filed April 1, 2009, providing arguments in support of the traversal. See pages 9-17. For the following reasons, Applicants' arguments are not persuasive.

i. Claims 11-12 and 15-17

Applicants traverse the combination of Mazet and Barbier on multiple grounds, and direct them mainly against the independent claim.

Applicants first cite to the purported objective of Mazet and opine that because this objective is different from that of the claimed invention, which is to “find improved methods of carrying out electrochemical studies on membrane bodies,” the skilled artisan would not have consulted Mazet. See page 11, third paragraph. Notably, the instant claims are not directed to an improved method or an electrochemical study. Moreover, the specification suggests that the invention is directed at a broader electrophysiological method. See page 1 (describing general study of “electrophysiological measurements”). Accordingly, because the claimed invention is not limited to an improvement or electrochemical phenomenon, Applicants’ arguments on this point is not convincing.

Applicants also argue that Barbier does not remedy the deficiency of Mazet in not teaching a membrane body for three reasons outlined on page 13. Responding to the first reason, although Barbier does not describe a lipid bilayer and a living cell membrane, this fact does not remove Barbier as an applicable reference. Indeed, if Barbier taught this configuration, then Mazet may not have been necessary as a reference. As described above, the rejection is based on the combination of Mazet and Barbier, the former providing the lipid bilayer and the latter providing the cell. Because the same type of gap junction is provided by both references, the skilled artisan would

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have found it obvious to substitute one of the membranes in Mazet with one of the cells in Barbier.

Responding to the second reason, the fact that Barbier is directed to biochemical and optical methods does not *per se* remove it as an applicable reference. Indeed, the connection between Mazet and Barbier is the connexin gap junction described by both references. Because the membranes and cells can form these junctions, it would have been obvious to for the junction between them, lacking evidence to the contrary. Applicants make a related argument on page 14 (third paragraph), directed at the motivation for combining Mazet and Barbier. For the same reason just described, because the two references describe the same type of gap junction, the skilled artisan would have found it obvious to apply a cell comprising connexins to the electrode measuring method taught by Mazet.

Responding to the third reason, the claims are not directed to a method of investigating the properties of membrane bodies, but instead to a method of measuring an electrical signal on a membrane body. Combined, Mazet and Barbier teach this method. A related argument is made on page 14 (third paragraph), alleging that Mazet and Barbier are directed to characterizing gap junctions and not that of membrane bodies. However, by including Barbier's cell with Mazet's method, the characterization would be on the cell. It is this aspect that the skilled artisan, reading both Mazet and Barbier, would have found obvious.

Applicants finally argue that a lipid bilayer would rupture when placed close to a cell, "long before any connexins found each other and interacted to form a stable gap

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junction.” Lacking any evidence of this allegation, Applicants’ argument is not convincing. Evidence of this phenomenon in a publication or in the form of an affidavit or declaration, however, may overcome the prior art rejection.

i. Claim 13

Applicants traverse the rejection of claim 13, arguing that Xu does not remedy the allegation that Mazet and Barbier are not properly combinable. See page 15, last paragraph. Applicants also opine that Xu is “irrelevant” because Xu is directed to “very early prior art” and directed to atomic force microscopy, which has a different goal from the instant application. See page 16, second paragraph.

As described above, Mazet and Barbier are properly combinable; hence, there is nothing for Xu to remedy. Moreover, one of the motivations for combining Xu with Mazet and Barbier is that conductances can be measured, which are electrical in nature and very relevant to the “electrical signal” as claimed. Finally, simply because a reference is old does not mean it is not good prior art. In fact, contentions that the reference patents are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977).

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2872. The examiner can normally be reached on Monday to Friday (8:30 am to 5:00 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon Y. Lum/
Examiner, Art Unit 1641

/Nelson Yang/
Primary Examiner, Art Unit 1641